REFERENCES

1. Sørensen R, Abildstrom SZ, Hansen PR, et al. Efficacy of post-operative clopidogrel treatment in patients revascularized with coronary artery bypass grafting after myocardial infarction. J Am Coll Cardiol 2011;57:1202–9.
2. Anderson JL, Adams CD, Antman EM, et al. ACC/AHA 2007 guidelines for the management of patients with unstable angina/non–ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction). J Am Coll Cardiol 2007;50:e1–157.
3. Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. N Engl J Med 2001;345:494–502.
4. Fox KA, Mehta SR, Peters R, et al. Benefits and risks of the combination of clopidogrel and aspirin in patients undergoing surgical revascularization for non-ST-elevation acute coronary syndrome: the Clopidogrel in Unstable angina to prevent Recurrent ischemic Events (CURE) trial. Circulation 2004;110:1202–8.
5. Kulik A, Chan V, Ruel M. Antiplatelet therapy and coronary artery bypass graft surgery: perioperative safety and efficacy. Expert Opin Drug Saf 2009;8:169–82.
6. Kulik A, Le May M, Wells GA, Mesana TG, Ruel M. The clopidogrel after surgery for coronary artery disease (CASCADE) randomized controlled trial: clopidogrel and aspirin versus aspirin alone after coronary bypass surgery [NCT00228423]. Curr Control Trials Cardiovasc Med 2005;6:15.
7. Kulik A, Le May MR, Voisine P, et al. Aspirin plus clopidogrel versus aspirin alone after coronary artery bypass grafting: the clopidogrel after surgery for coronary artery disease (CASCADE) trial. Circulation 2010;122:2680–7.

The Unknown Effect of Clopidogrel Resistance in Dual Antiplatelet Therapies After Coronary Artery Bypass Grafting

We read with great interest the article of Sørensen et al. (1) that reported the efficacy of post-operative clopidogrel treatment in a large patient cohort revascularized with coronary artery bypass graft surgery (CABG) after myocardial infarction. Notwithstanding the criterion of preoperative myocardial infarction, it remains interesting that this result is contrary to the CASCADE (Clopidogrel After Surgery for Coronary Artery DiseasE) trial, where addition of clopidogrel to aspirin revealed no changes on the post-operative outcomes (survival, 1-year intimal hyperplasia) (2). A possible explanation could be the different rates of aspirin and/or clopidogrel resistance between the 2 populations.

Aspirin resistance after cardiac surgery varies between 7% and 54% (depending on the platelet assay) (3). In contrast, clopidogrel response in patients undergoing CABG remains unknown due to the fact that aspirin is the drug of first choice after CABG, and clopidogrel administration (in addition to aspirin) is recommended mainly in patients with acute coronary syndrome (1). However, previous reports indicate that the clopidogrel resistance rate in coronary stent patients varies between 5% and 56% (4). Besides, carriers of defective alleles for *CYP2C19* and *CYP2C9* and patients undergoing omeprazole and atorvastatin therapy (inhibitors of *CYP2C19* and *CYP3A4*, respectively) are at risk of clopidogrel resistance as well (5).

Certainly, the considerably high prevalence of clopidogrel resistance in noncardiac surgery patients creates the necessity for assessment of clopidogrel nonresponders undergoing CABG. Otherwise, it remains unknown in dual antiplatelet therapies whether the response to clopidogrel covers a possible aspirin resistance or vice versa. Finally, we congratulate the authors for this excellent and well-defined study and for their contribution to the optimization of the clinical outcomes in patients undergoing CABG after myocardial revascularization.

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REFERENCES

1. Sørensen R, Abildstrøm SZ, Hansen PR, et al. Efficacy of post-operative clopidogrel treatment in patients revascularized with coronary artery bypass grafting after myocardial infarction. J Am Coll Cardiol 2011;57:1202–9.
2. Kulik A, Le May MR, Voisine P, et al. Aspirin plus clopidogrel versus aspirin alone after coronary artery bypass grafting: the clopidogrel after surgery for coronary artery disease (CASCADE) trial. Circulation 2010;122:2680–7.
3. Kasotakis G, Pipinos II, Lynch TG. Current evidence and clinical implications of aspirin resistance. J Vasc Surg 2009;50:1500–10.
4. Serebruany VL, Steinhubl SR, Berger PB, Malinin AI, Bhatt DL, Topol EJ. Variability in platelet responsiveness to clopidogrel among 544 individuals. J Am Coll Cardiol 2005;45:246–51.
5. Lau WC, Gurbel PA, Watkins PB, et al. Contribution of hepatic cytochrome P450 3A4 metabolic activity to the phenomenon of clopidogrel resistance. Circulation 2004;109:166–71.

Reply

We read with interest the letters by Drs. Kulik and Ruel and by Dr. Bisdas and colleagues commenting on our study about the efficacy of clopidogrel treatment in patients with myocardial infarction (MI) treated with coronary artery bypass graft surgery (CABG) (1).

Our study was a nationwide cohort study based on exact information from nationwide registers of claimed prescriptions and hospitalizations in Denmark. Although these registers include comprehensive data, some details are not listed, for example, on-pump/off-pump, whereas platelet function tests are currently not recommended for routine use (2). Including these variables might have increased the accuracy of our models, but we do not believe it would have changed the results substantially. Importantly, we found reduced mortality among patients receiving clopidogrel after CABG. This finding was consistent in the propensity-matched subgroup analysis. We did not find reduced recurrent MIs. However, contrary to the statement by Drs. Kulik and Ruel, we found reduced cardiovascular death among the